

**REMARKS**

The Office Action dated November 26, 2007 has been carefully considered.

Accordingly, the present Amendment is believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present amendment, claim 1 has been amended to recite controlling an overall proton concentration in a ring-opening polymerization system by adding water to the cyclic ester to control the over all proton concentration in the cyclic ester in accordance with the teachings of the specification at paragraphs [0019] and [0061]. It is believed that these changes do not involve any introduction of new matter, whereby entry of the amendments is believed to be in order and is respectfully requested.

Claims 1, 4, 6 and 10-22 were rejected under 35 U.S.C. §103(a) as being unpatentable over Shinoda et al (US 5,412,067) in view of Howelton et al (US 5,342,918) and the *Handbook of Thermoplastic Polymers*, Chapter 2, pages 80-94 (HTP). Claims 7-9 have been rejected under 35 U.S.C. §103(a) as being obvious and unpatentable over this combination of references and further in view of Early et al (US 6,437,565). Applicants respectfully traverse these rejections and request reconsideration of the patentability of claims 1, 4 and 6-22.

As defined by claim 1, the invention is directed to a process for producing an aliphatic polyester by subjecting a cyclic ester to bulk ring-opening polymerization. The process comprises providing a cyclic ester purified to the extent that a water content is at most 50 ppm, an  $\alpha$ -hydroxycarboxylic acid content is at most 100 ppm, and linear  $\alpha$ -hydroxycarboxylic acid oligomers content is at most 1000 ppm, and controlling an over all proton concentration in a ring-opening polymerization system by adding water to the cyclic ester. The overall protein concentration in the cyclic ester is calculated out on the basis of the total amount of hydroxycarboxylic compounds consisting of  $\alpha$ -hydroxycarboxylic acid and the linear  $\alpha$ -hydroxycarboxylic acid oligomer as impurities in the cyclic acid, water contained

as impurities in the cyclic ester, and water added to the cyclic ester. The process further comprises subjecting the cyclic ester to ring opening polymerization in a closed state, thereby controlling melt viscosity as the resulting aliphatic polyester. As described in the specification of the present application, "Therefore, the overall proton concentration is controlled by addition of water, whereby an aliphatic polyester having a targeted melt viscosity or molecular weight can be produced." (paragraph 0019). The invention of the present application is a significant invention in that an aliphatic polyester having a targeted melt viscosity or molecular weight can be produced by controlling the overall proton concentration.

It has been found that when an aliphatic polyester such as polyglycolic acid is produced by ring-opening polymerization of a cyclic ester such as glycolide using a high-purity cyclic ester and water is added to the cyclic ester to control the overall proton concentration in the cyclic ester, the melt viscosity and the molecular weight of the formed polymer can be precisely controlled. The overall proton concentration in the cyclic ester is determined by the amount of water and hydroxycarboxylic compounds contained as impurities and the added water. It has not previously been known that the melt viscosity and molecular weight of an aliphatic polyester can be controlled by controlling the overall proton concentration in the cyclic ester with the addition of water. As will be discussed in detail below with reference to the Examples and Comparative Examples in the present specification, the presently claimed process allows the production of aliphatic polyesters having good, precisely controlled melt viscosity, desired molecular weight, and low yellowing.

In the Official Action, the Examiner asserted that Shinoda discloses a preparation process of polyester with desirable MW (molecular weight) or melt viscosity (note, that melt viscosity of a resulting aliphatic polyester polymer is proportional function of the MW of the

polyester) from cyclic esters or their mixtures (referring to column 1, lines 5-15), wherein impurities such as water and hydroxycarboxylic acids (including oligomers) are accurately controlled (thus proton concentration also controlled) with total amount less than 100 ppm (see abstract, column 2, lines 40-68, column 3, line 5-7, and column 6, line 50) in order to produce polyester with desirable MW (see column 3, lines 1-5).

However, the teachings of Shinoda et al are recognized as prior art by the present inventors. The disclosure of Shinoda et al is cited in the specification of the present application as follows:

"In a production process of an aliphatic polyester by subjecting a cyclic ester to ring-opening polymerization, it is proposed to determine the amount of a hydroxyl group-containing compound added to a reaction system on the basis of the amount of free carboxylic compounds contained in the cyclic ester (for example, Japanese Patent No. 3075665). In this document, an  $\alpha$ -hydroxycarboxylic acid used upon the production of the cyclic ester and linear  $\alpha$ -hydroxycarboxylic acid oligomers are shown as the free carboxylic compounds, and the document describes that a monohydric linear saturated aliphatic alcohol having 12 to 18 carbon atoms is preferred as the hydroxyl group-containing compound.

Shinoda et al also indicate that when the impurities such as water and free carboxylic compounds are contained in the cyclic ester, the polymerization reaction is adversely affected, and so producing a polymer having a targeted molecular weight becomes impossible even under the same polymerization conditions. Shinoda et al disclose that since a high water content shows a tendency to make the control of a molecular weight of the resulting aliphatic polyester difficult, the water content in the cyclic ester is preferably controlled to at most 100 ppm for the purpose of controlling the molecular weight with good accuracy. Further, Shinoda et al indicate that although water in the cyclic ester can be easily removed in a purification and drying process just before the polymerization, the free carboxylic compounds are difficult to be removed, exert a great influence on the polymerization reaction, and moreover the cyclic ester is ring-opened by a minute amount of water during its storage to easily form new free carboxylic compounds. Shinoda et al propose to determine free carboxylic compounds contained in the cyclic ester and add a hydroxyl group-containing

compound (for example, higher alcohol) in an amount corresponding to this amount, thereby producing an aliphatic polyester having a targeted molecular weight.” (US 2006/0004183A1, paragraphs 0009-0011).

As described above, the disclosure of Shinoda et al was fully known by the present inventors. In the specification of the present application, the above description is followed by the following:

“As described above, the fact that a cyclic ester, from which impurities such as water and free carboxylic compounds have been removed, is used in a process for producing an aliphatic polyester by ring-opening polymerization of the cyclic ester, and an alcohol, particularly a higher alcohol is used as a molecular weight modifier was the state of the art.” (US 2006/0004183A1, paragraph 0012).

Thus, Shinoda et al was art overcome by the present inventors, and particularly, the Shinoda et al disclosure that in order to accurately control the molecular weight of polyester having a molecular weight of 100,000 or more in particular, moisture content of the cyclic ester compound is preferably 100 ppm by weight or less.” (US 5412067A, column 6, lines 46-50). Importantly, since Shinoda et al consider water as impurities, it is apparent that a person with ordinary skill in the art cannot find the addition of water obvious in view of the art disclosed in Shinoda et al because it would be illogical to increase an impurity.

Accordingly, it may safely be said that Shinoda et al contradict and teach away from the addition of water, and not, as the Examiner has asserted, that Shinoda is silent about addition of water to polymerization system. Accordingly, for this reason, Shinoda et al cannot be combined with Howelton et al's addition of water as asserted by the Examiner.

The Examiner has asserted that Shinoda discloses a process wherein polymer with desirable characteristics is obtained by controlling impurities that contribute to overall proton concentration.”. However, Shinoda et al consider the amount of the free carboxylic acid to be most important for obtaining polyester having a desirable molecular weight.

“According to the information of the present inventors, it has been known that, in the preparation of polyester having a molecular weight of , for example, tens of thousands-

hundreds of thousands, molecular weight of the formed polyester widely fluctuates in the presence of merely tens-100 ppm of free carboxylic acid." (US 5412067A, column 3, lines 1-6).

In order not to cause this free carboxylic acid to exist, Shinoda et al disclose:

"A preparation process of polyester by adding a hydroxyl compound as a molecular weight regulator to a reaction system and conducting ring-opening polymerization of a cyclic ester compound, comprising fixing an amount of the hydroxyl compound to be added to the reaction system on the basis of the amount of free carboxylic acid contained in the cyclic ester compound." (US 5412067A, claim 1); and

"The hydroxyl compound is one or more compounds selected from alcohol, hydroxycarboxylic acid and saccharide." (claim 2).

Since the amount of free carboxylic acid is most important for obtaining polyester having a desirable molecular weight, Shinoda et al thus disclose that alcohol, hydroxycarboxylic acid and saccharide are used. Shinoda et al do not teach, suggest or recognize the use of water for any improvement. On the basis of this fact, Shinoda et al disclose as follows:

"The cyclic ester compound used for the invention is preferably purified by recrystallizing from a solvent such as ethyl acetate. The cyclic ester compound used in the invention is preferably dehydrated as much as possible before subjecting to the polymerization reaction. When the moisture content is high, molecular weight control of polyester is liable to be difficult." (US 5412067A, column 6, lines 37-43).

This description only recommends the use of a cyclic ester compound low in content of impurities, and does not teach or suggest a process as presently claimed wherein polymer with desirable characteristics is obtained by controlling impurities that contribute to overall proton concentration. The specification of the present application describes that

"It has been a matter of common sense in technology that water is removed as impurities inhibiting the ring-opening polymerization of the cyclic ester. However, it has been surprisingly proved that water has an excellent action as a molecular weight control agent. When a small amount of water is added to, for example, glycolide to control the overall proton concentration in the glycolide within a range of a low level, polyglycolic acid having a high molecular weight and a high melt viscosity compared with the case where no molecular weight control agent is used, or a higher alcohol is used as a molecular weight control agent can be obtained." (US 2006/0004183A1, paragraph 0018).

In other words, claim 1 of the present application indicates that the overall proton concentration in a ring-opening polymerization system can be controlled by adding water,

which has come to be contradicted as impurities. This is a significant distinction in the process of claim 1 of the present application.

The Examiner has relied on Howelton et al as teaching addition of water (as polymerization initiator) in ring-opening polymerization (see column 1, line 20). However, Howelton et al do not disclose that the overall proton concentration is controlled in the production process for producing an aliphatic polyester by subjecting a cyclic ester to bulk ring-opening polymerization. Rather, Howelton et al disclose a process for producing carboxyl-terminated polyamides by the reaction of cyclic lactams and amino acids and only teach the addition of water as an initiator for the reaction. Howelton et al provide no teaching or suggestion relating to a ring-opening reaction of cyclic ester such as glycolide and lactide. Howelton et al disclose carboxyl-terminated polyetheramides made by capping polyetheramides (aminoacids) with cyclic lactams (US 5342918A, column 3, lines 25-28). Cyclic lactams have the structure of the formula shown on column 5 (US 5342918A1), and are not cyclic esters.

Thus, one of ordinary skill in the art would have found the cyclic lactams disclosed in Howelton et al to be significantly different from the cyclic ester of Shinoda et al and recited in claim 1 of the present application. A polyamide and an aliphatic polyester are entirely different polymers from each other. A person with ordinary skill in the art cannot be motivated so that technical items relating to the synthesis of the polyamide are applied to the production process of the aliphatic polyester as they are. The Examiner asserted that Howelton et al disclose that in one preparation technique, the polymerization of epsilon-caprolactam (also known as epsilon-aminocaprolactam or simply caprolactam) is carried out by adding water to open the ring and then removing water again at elevated temperature, where linear polymer forms (US 5342918A, column 1, lines 17-22). However, as described,

the water disclosed in Howelton et al is used for opening the ring of a cyclic compound such as caprolactam. The water is thus removed by subsequently raising the temperature.

This fact is apparent from the following Examples 1-4 of Howelton et al which describe that

"The reactor was charged with laurolactam and various carboxylic acids/amino acids (as specified in Table 1), 50 ml of deionized water and 0.25 grams of IRGANOX 1098. The reactants and water were charged then purged with nitrogen for 15 minutes followed by heating at 250°C. for 2 hours to allow ring opening of the lactam with water. Water was slowly vented off and reactants were held at 250°C. for one additional hour." (US 5342918A, column 6, lines 39-47).

Thus, in Howelton et al, water is added to the reaction system to allow ring opening of the cyclic lactam. Howelton et al neither disclose nor suggest anything that water is added to control the overall proton concentration in the ring-opening polymerization system. On the other hand, in the process according to the present invention, the ring-opening polymerization of the cyclic ester is conducted by using a ring-opening polymerization catalyst in accordance with a method known per se in the art. For example, in order to produce an aliphatic polyester using the cyclic ester, it is preferable to adopt a process comprising heating the cyclic ester to conduct ring-opening polymerization. This ring-opening polymerization process is substantially a bulk ring-opening polymerization process. The ring-opening polymerization is conducted at a temperature within a range of generally 100 to 270 degrees C, in the presence of a catalyst (US 2006/0004183A1, paragraph 0033). No water is added to allow ring opening of the cyclic ester. To the contrary, in the process according to the present invention, water is added to control the overall proton concentration in the ring-opening polymerization system.

In addition, Howelton et al do not specifically teach any relation between the amount of water and melt viscosity or molecular weight. Rather, Howelton et al only teach the addition of water as an initiator for the reaction in the process for producing carboxyl-

terminated polyamides by the reaction of cyclic lactams and amino acids. Thus, Howelton et al do not resolve the deficiencies of Shinoda et al.

Neither are the deficiencies of Shinoda et al resolved by HTP. The ring-opening polymerization of the cyclic ester as recited in claim 1 is performed in a closed state so that the overall proton concentration in the cyclic ester is prevented from changing by mixing of water (moisture) in an external atmosphere. In order to precisely control the melt viscosity of the aliphatic polyester according to the process of the present invention, it is necessary to strictly control the polymerization reaction system in such a manner that the overall proton concentration, including the added water, is retained to a predetermined value. In contrast, HTP only states a general theory as to ring-opening polymerization and does not suggest the fact that the overall proton concentration, including the amount of added water, in the cyclic ester should be precisely controlled by conducting the polymerization reaction system in a closed state.

Additionally, at pages 90-94 referred to by the Examiner, HTP describes ring-opening polymerizations for polycaprolactone and polylactide production. Importantly, on page 94, HTP discloses that the cyclic dimer will contain neither water nor linear oligomers for production of polylactide. Thus, HTP similarly teaches away from water addition. Further, while HTP indicates that the lack of volatile byproducts eliminates the requirement for a vacuum, Applicants find no teaching that the reaction should be conducted in a closed system as presently claimed, and Applicants particularly find no teaching or suggestion of the specific process steps and apparatus as recited in the present claims.

Early et al similarly fail to resolve the deficiencies of Shinoda et al and specifically fail to teach or suggest any relation between the overall proton concentration in the cyclic ester and the melt viscosity of the aliphatic polyester. In view of this deficiency in the teachings of Early et al, Shinoda et al, Howelton et al, and HTP, the combinations of these

references asserted by the Examiner provides no motivation to one of ordinary skill in the art to add water to the cyclic ester on the basis of a relational expression between a predetermined overall protein concentration in the cyclic ester and a melt viscosity of the aliphatic polyester.

The Examiner's attention is again directed to the Examples and Comparative Examples set forth in the present specification beginning at page 38. These Examples and Comparative Examples include a comparison which demonstrates the improvements in process and product provided by the claimed invention as compared with the exemplary teachings of Shinoda et al. More particularly, when 1-dodecyl alcohol (lauryl alcohol) as exemplified by Shinoda et al is added as the molecular weight control agent to conduct ring-opening polymerization of glycolide as shown in Comparative Example 3 in Table 1 of the present specification (page 43), the weight average molecular weight of polyglycolic acid formed can be controlled with a measure of accuracy. However, the amount of volatile matter (residual monomer) contained in the polyglycolic acid is high, namely 0.55% by weight. Since the polyglycolic acid in Comparative Example 3 contains the volatile matter (residual monomer) in a relatively high amount, the melt viscosity thereof is markedly low (1,560 Pa's), even though it is a high-molecular weight polymer (Mw = 181,000). In contrast, when water is added as the molecular weight control agent to glycolide so as to control the overall proton concentration to a predetermined value in the ring-opening polymerization as shown in Examples 1-4 in Table 1, polyglycolic acid having a desired corresponding high melt viscosity (3470-3630 Pa's) and weight average molecular weight (205,000-218,00) can be obtained. In addition, extremely little volatile matter is contained in the polyglycolic acid (0.01-0.11% by weight).

The Examiner previously stated that arguments directed to the amount of volatile matter are irrelevant to the claimed subject matter of claims 1 and 3-20. However, a

comparison of the results of Comparative Example 3 with the results of Examples 1-4 shows that when a higher alcohol such as lauryl alcohol as exemplified by Shinoda et al is used as the molecular weight control agent (Comparative Examples), the weight average molecular weight of the resulting polymer can be controlled with a measure of accuracy, but a melt viscosity value corresponding to the value of the weight average molecular weight cannot be obtained. Rather, a low melt viscosity undesirably results. As the cause thereof, Table 1 of the present specification shows that the amount of volatile matter (residual monomer) is high in the product of the Comparative Example 3 process using lauryl alcohol, particularly as compared with the products produced by the processes of Examples 1-4, in which water is added to control the overall proton concentration and low volatile matter results.

Accordingly, the amount of volatile matter is a measure of the unexpected improvement provided by the process of the present invention, with the desirable low volatile matter allowing better control of the melt viscosity of a resulting aliphatic polyester, in particular, allowing production of a high molecular weight aliphatic polyester having a correspondingly high melt viscosity as compared with the use of lauryl alcohol as exemplified by Shinoda et al.

Further, the results in Table 2 of the present specification (page 50) show that the amount of volatile matter in a ring-opening aliphatic polymer is high even when no water is added (Comparative Example 4). Therefore, the ring-opening polymer of Comparative Example 4 has an extremely low melt viscosity, 1,500 Pa·s, though it has the same weight average molecular weight (198,000) as the ring-opening polymer of Example 6 produced by adding water. However, the melt viscosity of the ring-opening polymer of Example 6 is 2,550 Pa·s, and it is apparent in view of the results of Examples 5, 7 and 8 that a good melt viscosity value corresponding to the weight average molecular weight value is attained according to the presently claimed process.

Moreover, although Applicants submit that the Examiner has not established a prima facie case of obviousness based on Shinoda et al, even in view of Howelton et al, HTP and Early et al, the showings set forth in the Examples and Comparative Examples of the present application rebut any prima facie case of obviousness established by the Examiner. That is, the results of Examples 1 to 4 in Table 1 and 5 to 8 in Table 2 of the present specification, according to the process of the present invention, show ring-opening polyglycolic acids having the intended melt viscosity can be obtained by adding water as claimed. In addition, Examples 7 and 8 particularly show a tendency to remarkably improve the yellowness index (YI), even in a region wherein the melt viscosity and weight average molecular weight are relatively low, when water is used as the molecular weight control agent. A ring-opening polymer low in both melt viscosity and yellowness index (YI) is desirable for use as a polymer for injection molding. Finally, Comparative Example 3 in Table 1 of the present specification shows that the yellowness index (YI) of the ring-opening polymer formed when lauryl alcohol is added as the molecular weight control agent is high compared with that of the ring-opening polymers (Examples 6 and 7 in Table 2) each having a similar weight average molecular weight.

When an applicant demonstrates substantially improved results and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary, *In re Soni*, 34 U.S.P.Q. 2d 1684, 1688 (Fed. Cir. 1995). The Examples and Comparative Examples set forth in the present specification demonstrate substantially improved results provided by the process according to the present invention, Applicants have stated that the results were unexpected, and the Examiner has not provided any evidence to the contrary. Thus, Applicants have rebutted any prima facie case of obviousness based on Shinoda et al.

The unexpected improvements in melt viscosity, molecular weight and yellowness index control in the aliphatic polyesters produced by the process of claim 1 are not suggested from the teaching of Shinoda et al, and the deficiencies of Shinoda et al are not resolved by the teachings of Howelton et al. That is, Howelton et al disclose a process for producing carboxyl-terminated polyamides by the reaction of cyclic lactams and amino acids and teach the addition of water as an initiator for the reaction. However, a polyamide as taught by Howelton et al and the aliphatic polyesters which are the subject of Shinoda et al and the present invention are entirely different polymers. A person of ordinary skill in the art would have had no motivation, absent the present specification, to use technical features relating to the synthesis of Howelton et al's polyamide in the production process of an aliphatic polyester as taught by Shinoda et al.

Moreover, as described above, Shinoda et al teach that the cyclic ester compound is preferably dehydrated as much as possible before the polymerization reaction. Thus, Shinoda et al positively exclude a process as presently claimed in which water is added to the reaction system of the ring-opening polymerization of the cyclic ester. Accordingly, a person of ordinary skill in the art would have had no motivation to combine the teachings of Shinoda et al with the teachings of Howelton et al.

The Examiner's effort to establish obviousness by showing that the addition of water may be found somewhere in the prior art, namely in the polyamide production of Howelton et al, is unavailing; in determining obviousness, the inquiry is not whether each element existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed. *Grain Processing v. American Maize*, 5 U.S.P.Q. 2d 1788, 1793 (Fed. Cir. 1988). Not only do Howelton et al fail to teach the addition of water to a cyclic ester, Howelton et al fail to teach or suggest improvements provided by the present process in

controlling the melt viscosity of aliphatic polyesters. Accordingly, the cited prior art does not make the present invention as a whole obvious.

It is therefore submitted that the processes defined by present claims 1, 4 and 6-22 are nonobvious over and patentably distinguishable from the cited combinations of Shinoda et al, Howelton et al, and HTP, or these references in further combination with Early et al, whereby the rejections under 35 U.S.C. §103 have been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Official Action and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Please charge any fees required in connection with the present communication, or credit any overpayment, to Deposit Account No. 503915.

Respectfully submitted,

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